# Viral-host interactions affecting neural differentiation of human progenitors

## Grant Award Details

Viral-host interactions affecting neural differentiation of human progenitors

**Grant Type:** Basic Biology III

**Grant Number:** RB3-05219

**Project Objective:** The overall goal of this project is to determine the effects of HCMV infection on neural lineage specification and maturation of neural progenitor cells. Studies are designed to the molecular basis of host-viral interactions leading to neural defects.

**Investigator:**

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| **Name:** | Deborah Spector |
| **Institution:** | University of California, San Diego |
| **Type:** | PI |

**Disease Focus:** Infectious Disease, Neurological Disorders, Pediatrics

**Human Stem Cell Use:** Embryonic Stem Cell

**Award Value:** $1,372,660

**Status:** Closed

## Progress Reports

**Reporting Period:** Year 1

**View Report**

**Reporting Period:** Year 2

**View Report**

**Reporting Period:** Year 3

**View Report**

## Grant Application Details

**Application Title:** Viral-host interactions affecting neural differentiation of human progenitors

**Public Abstract:**

Human cytomegalovirus (HCMV) is the major cause of birth defects, almost all of which are neuronal in origin. Approximately 1% of newborns are infected, and of the 13% that are symptomatic at birth, 50% will have severe permanent hearing deficits, vision loss, motor impairment, and mental retardation. At least 14% of asymptomatic infants also will later show disabilities. Much of this effect is likely caused by HCMV affecting neural development in the fetus.

Embryonic stem cells are an excellent source of human progenitors, which are cells that can turn into mature neurons i.e. neural differentiation. We know from published cell culture studies that HCMV affects neural progenitor cells during neural differentiation, but it is unclear as to what are the underlying molecular mechanisms for its effect. A major goal of our research is to understand at a high-resolution how HCMV controls the way neural progenitors become proper neurons. Elucidation of the genes that are affected will serve as a basis for therapeutic strategies to ameliorate the effects of HCMV infection in newborns.

The significance of our studies also extends to the serious problem of HCMV infection in immunocompromised individuals, with recipients of allogeneic transplants having a high risk of severe disease and allograft rejection. This potential problem in stem cell therapy has received little attention thus far. The proposed use of stem cell transplantation in treating neuronal injury and neurodegenerative diseases, as well as transplantation of other organ-specific precursors, makes it imperative to understand how disseminated HCMV infection in immunosuppressed recipients will affect the function and differentiation of the cells.

**Statement of Benefit to California:**

Human cytomegalovirus (HCMV) is the major viral cause of birth defects. In 2009, there were 526,774 births in California, resulting in congenital HCMV infection in approximately 5,200 newborns, with at least 800 infants expected to have long-lasting disabilities. Congenital cytomegalovirus infection is the most common nongenetic congenital cause of deafness. In contrast, before the development of the rubella vaccine, less than 70 infants per year in the entire US were reported to have congenital rubella syndrome, also associated with deafness. The burden to families and the economic costs to society of congenital cytomegalovirus infection are immense, and there is no vaccine available. Our proposed research serves to form the basis of future therapies to ameliorate, or even reduce this medical burden.

The significance of our studies also extends to the serious problem of HCMV infection in immunocompromised individuals who receive transplants of organs and stem cells from other individuals. Infection in these transplant recipients often results in severe disease and rejection of the transplant. The California Institute for Regenerative Medicine has made a major commitment to provide funding to move stem cell-based therapies to clinical trials. The goal of using stem cell transplantation to treat neuronal injury and neurodegenerative diseases, as well as transplantation of other organ-specific precursors, makes it imperative to understand how disseminated HCMV infection in immunosuppressed recipients will affect the function and differentiation of the cells.

Our research will provide the knowledge base to understand the genes that are changed during HCMV infection of human neural progenitors and neurons. It will also provide a foundation for studies of how other viruses will affect human neurons, and likely, other cell-types. Intellectual property from this work will feed into opportunities for antiviral strategies and increased jobs in biotech for Californians.